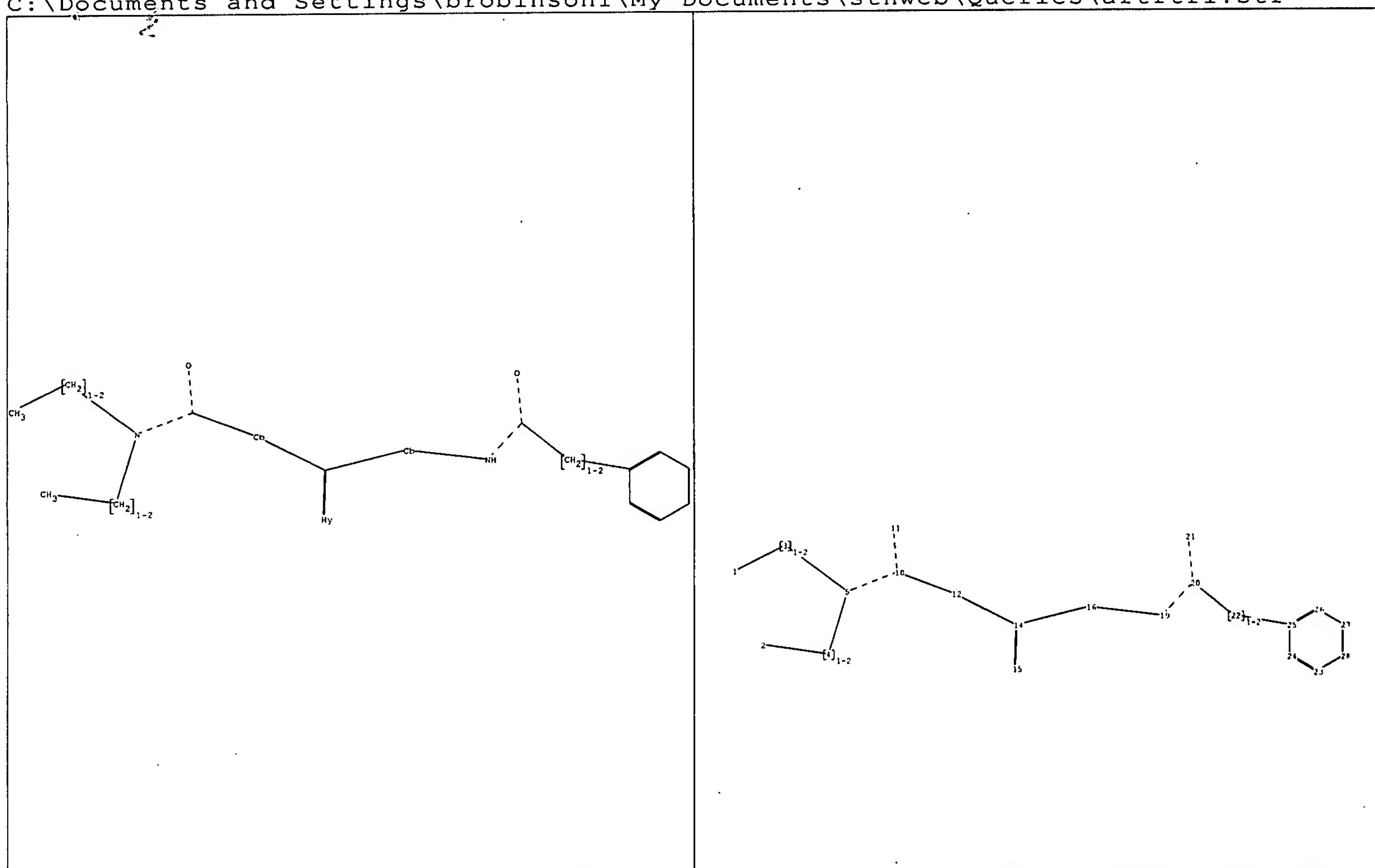


EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|-------|------|---|-----------------|------------------|---------|------------------|
| L1 | 1129 | ((546/234) or (546/212) or (546/214)).CCLS. | US-PGPUB; USPAT | OR | OFF | 2007/05/11 19:36 |
| L2 | 59 | 1 and benzamide and phenyl and piperidin | US-PGPUB; USPAT | OR | OFF | 2007/05/11 19:37 |
| L3 | 156 | (brown adj william.inv.) | US-PGPUB | OR | OFF | 2007/05/11 19:38 |
| L4 | 19 | (griffin adj andrew.inv.) | US-PGPUB | OR | OFF | 2007/05/11 19:41 |
| L5 | 156 | (brown adj william.inv.) | US-PGPUB | OR | OFF | 2007/05/11 19:41 |



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chain nodes :
 1 2 3 4 5 10 11 12 14 15 16 19 20 21 22
ring nodes :
 23 24 25 26 27 28
chain bonds :
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 20-21 20-22 22-25
ring bonds :
 23-24 23-28 24-25 25-26 26-27 27-28
exact/norm bonds :
 5-10 10-11 14-15 19-20 20-21
exact bonds :
 1-3 2-4 3-5 4-5 10-12 12-14 14-16 16-19 20-22 22-25
normalized bonds :
 23-24 23-28 24-25 25-26 26-27 27-28
isolated ring systems :
  containing 15 : 23 :

Match level :
 1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 10:CLASS 11:CLASS 12:Atom
 14:CLASS 15:Atom 16:Atom 19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:Atom
 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom
Generic attributes :
12:
  Saturation : Unsaturated
  Type of Ring System : Monocyclic
15:
  Saturation : Saturated
  Number of Carbon Atoms : less than 7
  Number of Hetero Atoms : Exactly 1
  Type of Ring System : Monocyclic
16:
  Saturation : Unsaturated

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Number of Carbon Atoms : less than 7
Type of Ring System : Monocyclic

Element Count :

Node 12: Limited
C, C6

Node 15: Limited
C, C5
N, N1

Node 16: Limited
C, C6

10533838

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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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| NEWS | 2 | JAN 08 CHEMLIST enhanced with New Zealand Inventory of Chemicals |
| NEWS | 3 | JAN 16 CA/CAplus Company Name Thesaurus enhanced and reloaded |
| NEWS | 4 | JAN 16 IPC version 2007.01 thesaurus available on STN |
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| NEWS | 7 | JAN 22 CA/CAplus enhanced with patent applications from India |
| NEWS | 8 | JAN 29 PHAR reloaded with new search and display fields |
| NEWS | 9 | JAN 29 CAS Registry Number crossover limit increased to 300,000 in multiple databases |
| NEWS | 10 | FEB 15 PATDPASPC enhanced with Drug Approval numbers |
| NEWS | 11 | FEB 15 RUSSIAPAT enhanced with pre-1994 records |
| NEWS | 12 | FEB 23 KOREAPAT enhanced with IPC 8 features and functionality |
| NEWS | 13 | FEB 26 MEDLINE reloaded with enhancements |
| NEWS | 14 | FEB 26 EMBASE enhanced with Clinical Trial Number field |
| NEWS | 15 | FEB 26 TOXCENTER enhanced with reloaded MEDLINE |
| NEWS | 16 | FEB 26 IFICDB/IFIPAT/IFIUDB reloaded with enhancements |
| NEWS | 17 | FEB 26 CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases |
| NEWS | 18 | MAR 15 WPIDS/WPIX enhanced with new FRAGHITSTR display format |
| NEWS | 19 | MAR 16 CASREACT coverage extended |
| NEWS | 20 | MARPAT now updated daily |
| NEWS | 21 | MAR 22 LWPI reloaded |
| NEWS | 22 | MAR 30 RDISCLOSURE reloaded with enhancements |
| NEWS | 23 | APR 02 JICST-EPLUS removed from database clusters and STN |
| NEWS | 24 | APR 30 GENBANK reloaded and enhanced with Genome Project ID field |
| NEWS | 25 | APR 30 CHEMCATS enhanced with 1.2 million new records |
| NEWS | 26 | APR 30 CA/CAplus enhanced with 1870-1889 U.S. patent records |
| NEWS | 27 | APR 30 INPADOC replaced by INPADOCDB on STN |
| NEWS | 28 | MAY 01 New CAS web site launched |
| NEWS | 29 | MAY 08 CA/CAplus Indian patent publication number format defined |
| NEWS EXPRESS | | NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006. |

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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10533838

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COST IN U.S. DOLLARS
SINCE FILE
ENTRY
TOTAL
SESSION
0.21
0.21
FULL ESTIMATED COST

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DICTIONARY FILE UPDATES: 10 MAY 2007 HIGHEST RN 934586-26-2

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1.1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -      43154 TO ITERATE
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4.6% PROCESSED 2000 ITERATIONS 1 ANSWERS

Updated Search

10533838

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 850675 TO 875485
PROJECTED ANSWERS: 153 TO 709

L2 1 SEA SSS SAM L1

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DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
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96.8% PROCESSED 835711 ITERATIONS 10 ANSWERS
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L3 10 SEA SSS FUL L1

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COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
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FILE COVERS 1907 - 11 May 2007 VOL 146 ISS 21
FILE LAST UPDATED: 1 May 2007 (20070501/ED)

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This file contains CAS Registry Numbers for easy and accurate

=> s 13
L4 2 L3

=> d 14, ibib abs hitstr, 1-2

L4 ANSWER 1 OF 2 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1016017 HCPLUS
DOCUMENT NUMBER: 142:6430

Updated Search

10533838

TITLE: Preparation of diarylmethylidene piperidine derivatives as opioid δ receptor ligands for treating pain, anxiety and functional gastrointestinal disorders

INVENTOR(S): Brown, William L.; Griffin, Andrew; Jin, Shujuan

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 131 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

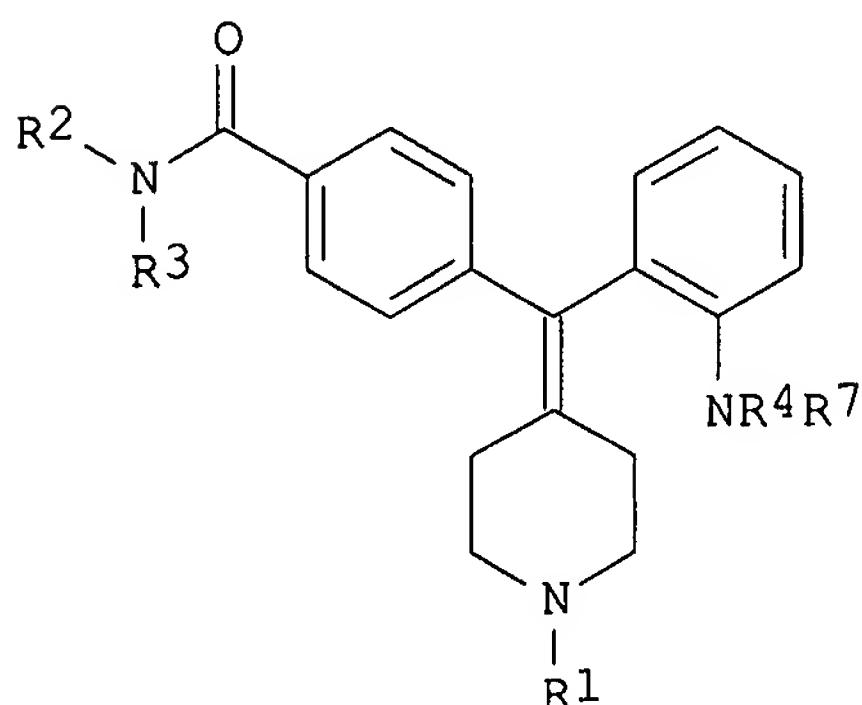
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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| WO 2004101522 | A1 | 20041125 | WO 2004-GB2074 | 20040513 |
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| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004238618 | A1 | 20041125 | AU 2004-238618 | 20040513 |
| CA 2525860 | A1 | 20041125 | CA 2004-2525860 | 20040513 |
| EP 1641757 | A1 | 20060405 | EP 2004-732665 | 20040513 |
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| BR 2004010347 | A | 20060530 | BR 2004-10347 | 20040513 |
| CN 1823040 | A | 20060823 | CN 2004-80020330 | 20040513 |
| JP 2007503457 | T | 20070222 | JP 2006-530500 | 20040513 |
| US 2007099957 | A1 | 20070503 | US 2005-555980 | 20051108 |
| NO 2005005998 | A | 20060213 | NO 2005-5998 | 20051216 |
| PRIORITY APPLN. INFO.: | | | SE 2003-1444 | A 20030516 |
| | | | SE 2004-24 | A 20040109 |
| | | | WO 2004-GB2074 | W 20040513 |

OTHER SOURCE(S): MARPAT 142:6430
GI



AB The title compds. [I; R1 = H, (un)substituted alkyl, aryl, etc.; R2-R4 = H, (un)substituted alkyl, cycloalkyl; R7 = H, OH, alkyl, etc.] which are useful in therapy, in particular in the management of pain, were prepared. E.g., a multi-step synthesis of I [R1 = H; R2, R3 = Et; R4 = COPh; R7 = H], starting from Me 4-(bromomethyl)benzoate, was given. The compds. I were found to be active toward human δ receptors. Generally, for most of the compds. I the IC50 values are in the range of 0.48 nM to 17.9 nM. The pharmaceutical composition comprising the compound I is disclosed.

IT 798549-18-5P 798549-19-6P 798549-23-2P

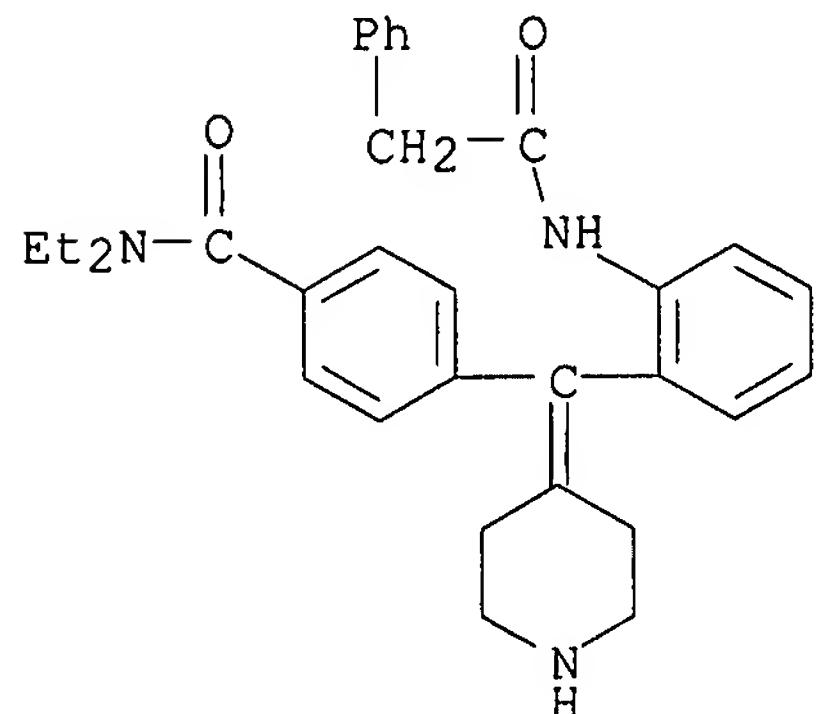
798549-24-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of diarylmethylidene piperidine derivs. as opioid δ receptor ligands for treating pain, anxiety and functional gastrointestinal disorders)

RN 798549-18-5 HCPLUS

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RN 798549-19-6 HCPLUS

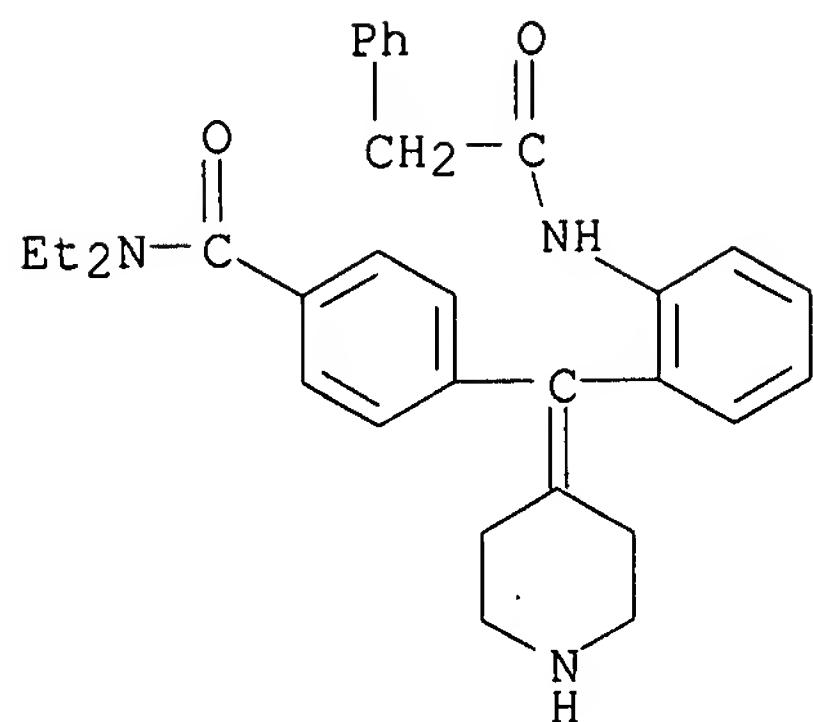
CN Benzeneacetamide, N-[2-[[4-[(diethylamino)carbonyl]phenyl]-4-piperidinylidenemethyl]phenyl]-, trifluoroacetate (10:11) (9CI) (CA INDEX NAME)

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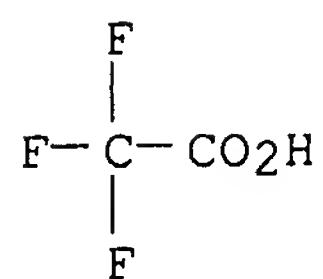
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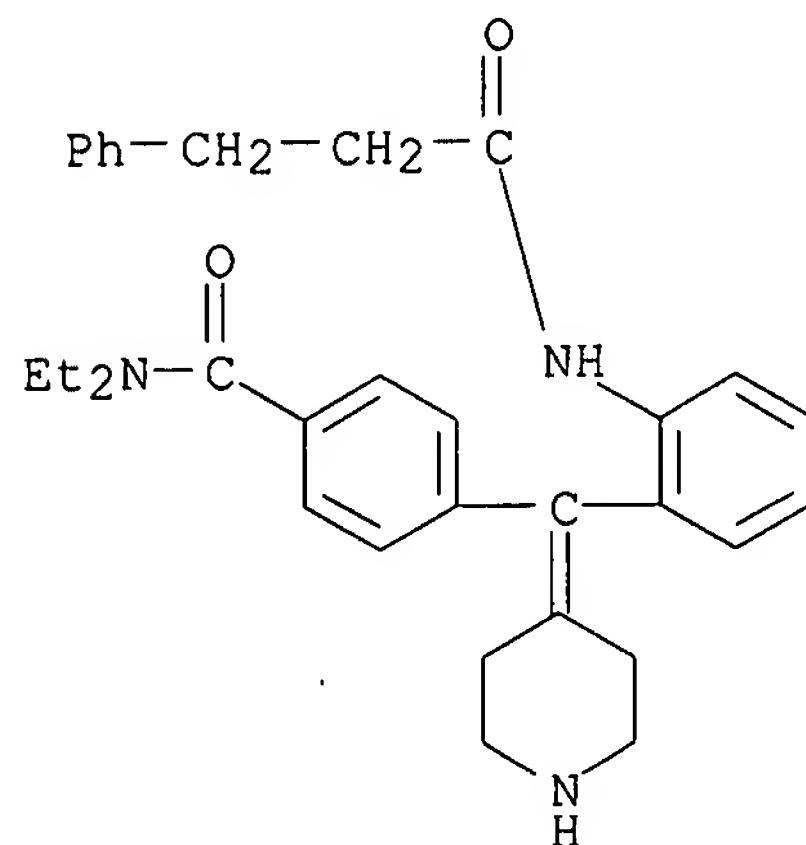


CM 2

CRN 76-05-1
CMF C2 H F3 O2



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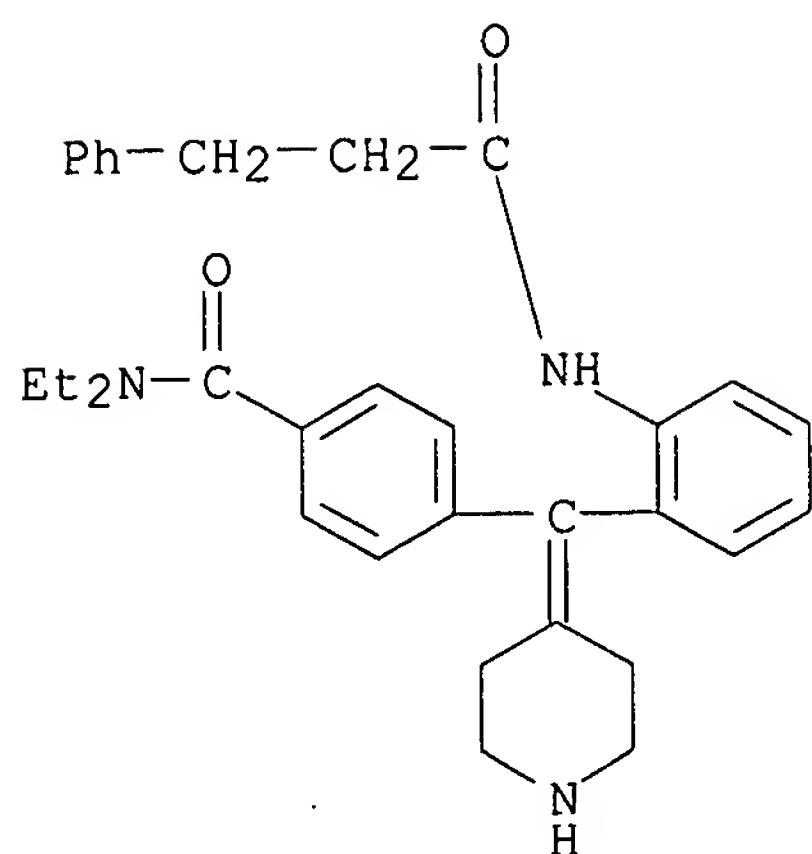
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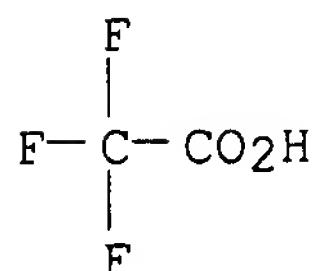
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CMF C32 H37 N3 O2



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:412920 HCPLUS
DOCUMENT NUMBER: 140:423590
TITLE: Preparation of 4-(phenylpiperidin-4-ylidenemethyl)benzamides for treatment of pain, anxiety, or gastrointestinal disorders
INVENTOR(S): Brown, William; Griffin, Andrew
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2004041784 | A1 | 20040521 | WO 2003-SE1705 | 20031105 |
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10533838

OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
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BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
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US 2006014789 A1 20060119 US 2005-533838 20050504
US 2002-3301 A 20021107
WO 2003-SE1705 W 20031105
PRIORITY APPLN. INFO.: .

OTHER SOURCE(S): MARPAT 140:423590
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein R1 = (un)substituted alkyl, cycloalkyl(alkyl), (hetero)aryl, R8CO, R8SO₂, R8SO, R8NHCO, R8CS, or R8NHCS; ; R2 = H or (un)substituted alkyl; R3 = H or (un)substituted alkoxy carbonyl, alkyl, or cycloalkyl(alkyl); R8 = (un)substituted alkyl, (hetero)aryl(alkyl), or cycloalkyl(alkyl); or pharmaceutically acceptable salts thereof] were prepared as opioid δ receptor ligands. For example, reaction of 4-(bromomethyl)benzoic acid Me ester with P(OMe)₃, followed by addition of 1-(tert-butoxycarbonyl)-4-piperidone in the presence of LDA in THF, gave 4-(4-methoxycarbonylbenzylidene)piperidine-1-carboxylic acid tert-Bu ester (35%). Addition of Br₂ (78%) and reaction with NaOH in MeOH provided 4-[bromo(4-carboxyphenyl)methylene]piperidine-1-carboxylic acid tert-Bu ester (87%). Conversion to the benzoyl chloride with iso-Bu chloroformate and amidation (73%) with Et₂NH in the presence of TEA in CH₂Cl₂, followed by coupling with 3-aminophenylboronic acid using Pd(PPh₃)₄ and Na₂CO₃ in toluene/EtOH/H₂O afforded N,N-diethyl-4-[(3-aminophenyl)(piperidin-4-ylidene)methyl]benzamide (97%). Alkylation of the amine with benzaldehyde and NaBH(OAc)₃ in 1,2-dichloroethane gave II. In binding assays using human 293S cells expressing cloned human opioid receptors and neomycin resistance, most compds. of the invention exhibited activity toward the δ receptor with IC₅₀ values in the range of 0.14 nM - 31.2 nM. Exemplified compds. also showed some activity toward the κ and μ receptors with IC₅₀ values in the ranges of 36 nM - 9680 nM and 3 nM - 5975 nM, resp. Thus, I and their pharmaceutical compns. are useful in therapy, in particular for the treatment of gastrointestinal disorders, anxiety, or pain (no data).

IT 692245-61-7P 692245-73-1P 692245-77-5P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(δ receptor agonist; preparation of (phenylpiperidinylidenemethyl)benz amides as δ receptor agonists for treatment of pain, anxiety, or gastrointestinal disorders)

RN 692245-61-7 HCPLUS

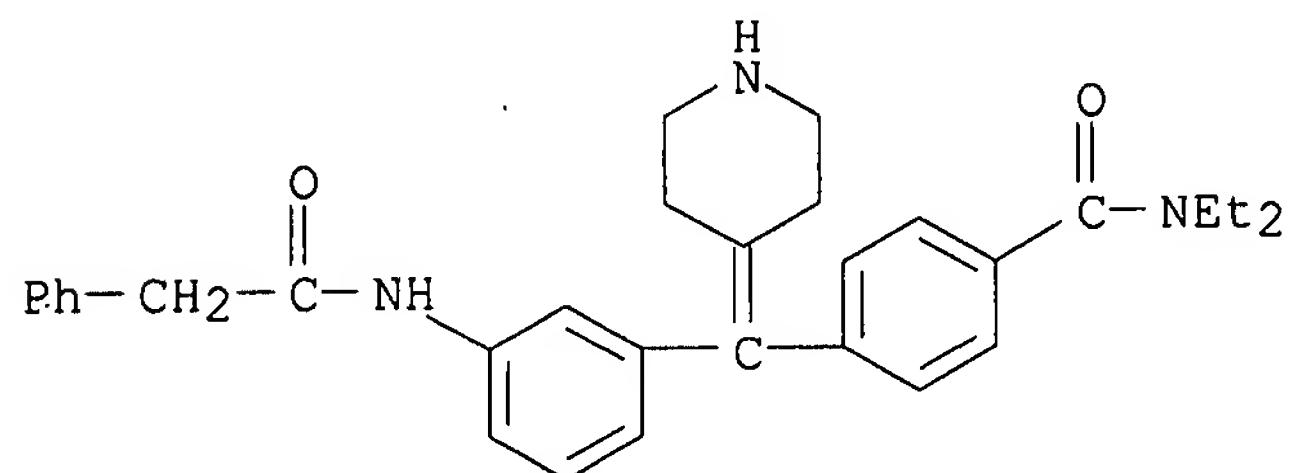
CN Benzeneacetamide, N-[3-[[4-[(diethylamino)carbonyl]phenyl]-4-piperidinylidenemethyl]phenyl]-, trifluoroacetate (5:9) (9CI) (CA INDEX NAME)

10533838

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CRN 692245-59-3

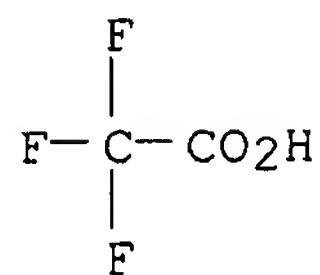
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CM 2

CRN 76-05-1

CMF C2 H F3 O2



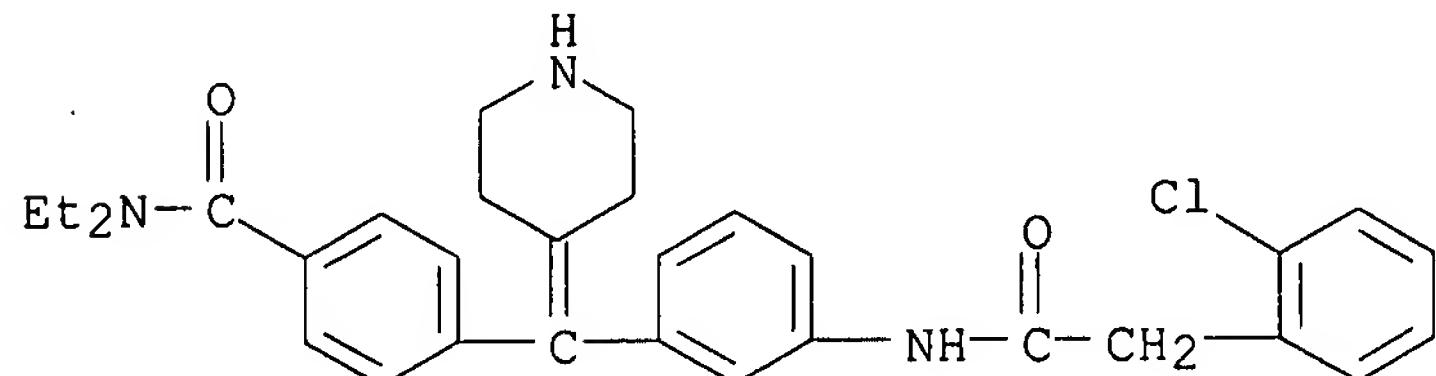
RN 692245-73-1 HCPLUS

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CRN 692245-71-9

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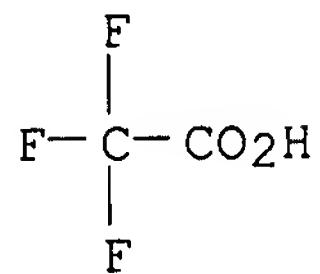
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CMF C2 H F3 O2

Updated Search

10533838



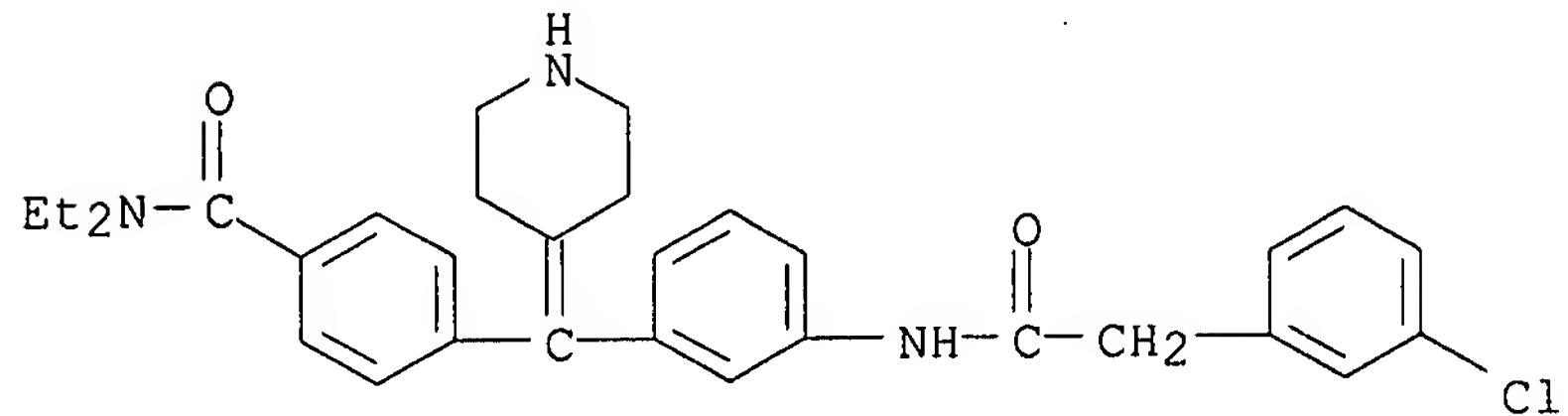
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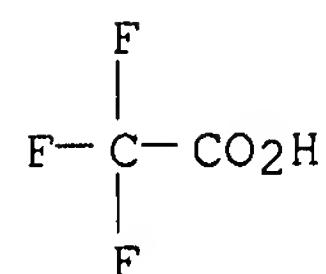
CMF C31 H34 Cl N3 O2



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 692245-59-3P, N,N-Diethyl-4-[[3-[(phenylacetyl)amino]phenyl](piperidin-4-ylidene)methyl]benzamide 692245-71-9P, 4-[[3-[(2-Chlorophenyl)acetyl]amino]phenyl](piperidin-4-ylidene)methyl]-N,N-diethylbenzamide 692245-75-3P, 4-[[3-[(3-Chlorophenyl)acetyl]amino]phenyl](piperidin-4-ylidene)methyl]-N,N-diethylbenzamide

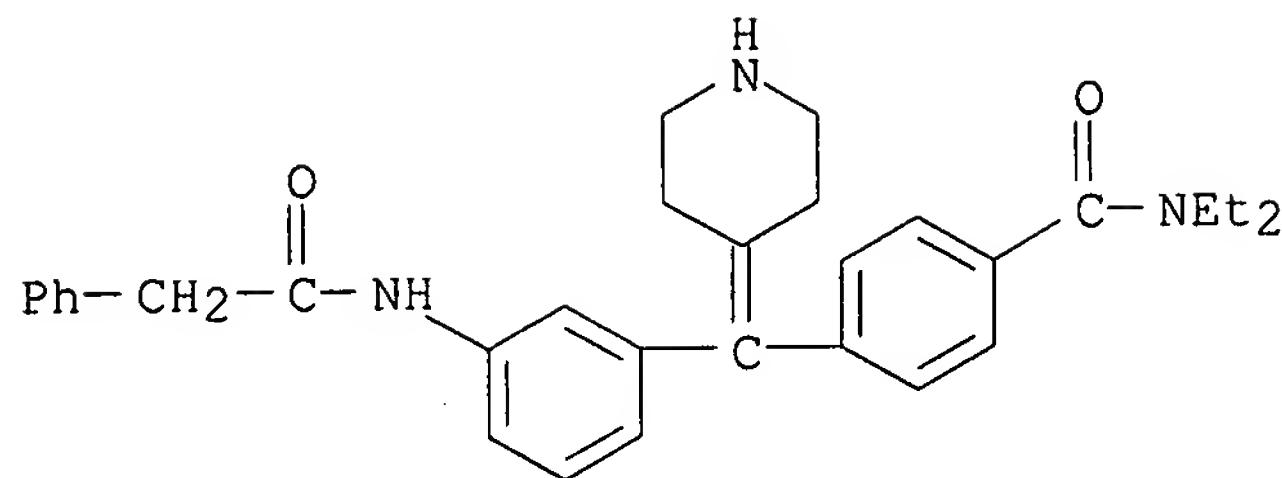
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(δ receptor agonist; preparation of (phenylpiperidinylidenemethyl)benzamides as δ receptor agonists for treatment of pain, anxiety, or gastrointestinal disorders)

RN 692245-59-3 HCPLUS

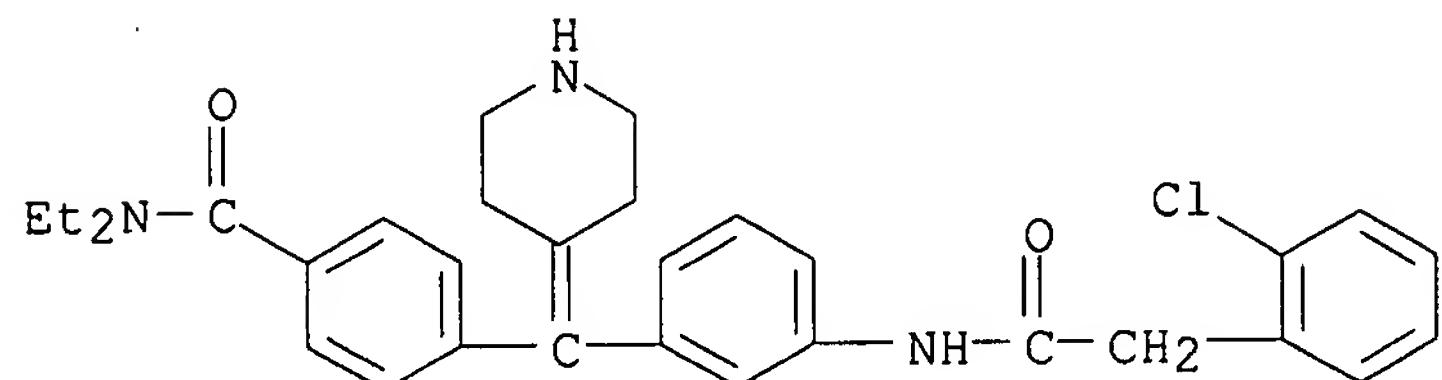
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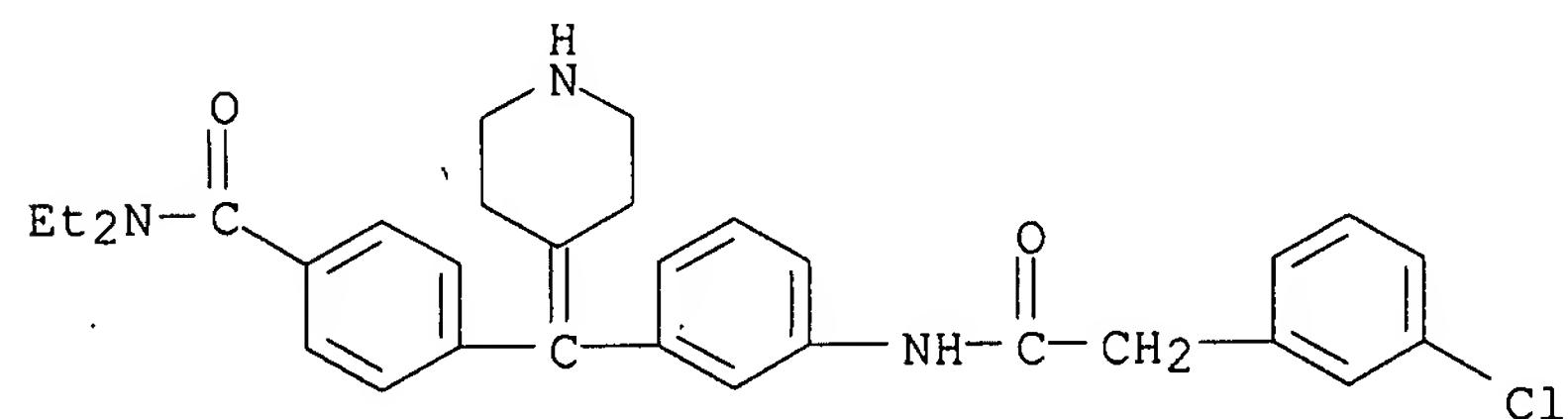
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CN Benzeneacetamide, 2-chloro-N-[3-[(4-[(diethylamino)carbonyl]phenyl]-4-piperidinylidenemethyl]phenyl]- (9CI) (CA INDEX NAME)



RN 692245-75-3 HCPLUS

CN Benzeneacetamide, 3-chloro-N-[3-[(4-[(diethylamino)carbonyl]phenyl]-4-piperidinylidenemethyl]phenyl]- (9CI) (CA INDEX NAME)



=> file caold
COST IN U.S. DOLLARS

| SINCE FILE ENTRY | TOTAL SESSION |
|---------------------|------------------|
| 13.14 | 189.95 |

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

| SINCE FILE ENTRY | TOTAL SESSION |
|---------------------|------------------|
| -1.56 | -1.56 |

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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

Updated Search

10533838

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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L1 STRUCTURE UPLOADED

L2 1 S L1

L3 10 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 16:38:59 ON 11 MAY 2007

L4 2 S L3

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=> s 13

L5 0 L3